

IN THE CLAIMS:

1. (withdrawn) An isolated nucleic acid encoding a peptide comprising a ZA loop of a bromodomain, said bromodomain having between about 21 to 40 amino acids, and wherein said bromodomain comprises the amino acid sequence of SEQ ID NO:3 and/or SEQ ID NO:48.

2. (withdrawn) The isolated nucleic acid of Claim 1 further comprising a heterologous nucleotide sequence.

3. (withdrawn) An isolated nucleic acid encoding a peptide comprising a ZA loop of a bromodomain, said bromodomain having between about 21 to 40 amino acids, and wherein said bromodomain has an amino acid sequence selected from the group consisting of SEQ ID NOs. 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, and 42.

4. (withdrawn) The isolated nucleic acid of Claim 3 further comprising a heterologous nucleotide sequence.

5. (currently amended) An isolated peptide consisting of a ZA loop of a bromodomain, said ZA loop of said bromodomain having between about 21 to 40 amino acids, and wherein said ZA loop of said bromodomain consists of an amino acid sequence selected from the group consisting of SEQ ID NOs. 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, ~~19~~, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, and 42, and the ZA loop of SEQ ID NO: 19.

6. (currently amended) A fusion protein or peptide consisting of a first sequence consisting of a ZA loop of a bromodomain according to one of SEQ ID NOs. 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, ~~19~~, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, and 42, and the ZA loop of SEQ ID NO: 19, and a second sequence from another protein.

7. (canceled)

8. (canceled)

9. (withdrawn) An antibody raised against the peptide of Claim 7 or raised against an antigenic fragment thereof.

10. (withdrawn) An antibody raised against the peptide of Claim 5.

11. (withdrawn) A method of identifying a compound that modulates the affinity of a bromodomain for a ligand that comprises an acetyl-lysine or an analog of acetyl-lysine, said method comprising:

(a) contacting the bromodomain and the ligand in the presence of the compound, wherein the bromodomain and the ligand bind in the absence of the compound; and

(b) measuring the affinity of the bromodomain for the ligand; wherein a compound is identified as a compound that modulates the affinity of the bromodomain for the ligand when there is a change in the affinity of the bromodomain for the ligand in the presence of the compound.

12. (withdrawn) The method of Claim 11, wherein the affinity of the bromodomain for the ligand increases in the presence of the compound and wherein the compound is identified as a bromodomain-ligand complex promoting agent.

13. (withdrawn) The method of Claim 11, wherein the affinity of the bromodomain for the ligand decreases in the presence of the compound and the compound is identified as an inhibitor.

14. (withdrawn) The method of Claim 11, wherein the compound is selected by performing rational drug design with the set of atomic coordinates obtained from one or more of Tables 1-6, wherein said selecting is performed in conjunction with computer modeling.

15. (withdrawn) The method of Claim 11, wherein the compound is selected by performing rational drug design with the set of atomic coordinates obtained from a set of atomic coordinates defining the three-dimensional structure of a bromodomain consisting of the amino acid sequence of SEQ ID NO:7, wherein said selecting is performed in conjunction with computer modeling.

16. (withdrawn) A method of identifying a compound that modulates the stability of a bromodomain-ligand binding complex comprising:

(a) contacting a bromodomain-ligand binding complex in the presence of the compound, wherein the bromodomain-ligand binding complex forms in the absence of the compound; and wherein the ligand comprises either an acetyl-lysine or an analog of acetyl-lysine; and

(b) measuring the stability of the bromodomain-ligand binding complex; wherein a compound is identified as a compound that modulates the stability of the bromodomain-ligand binding complex, when there is a change in the stability of the bromodomain-ligand binding complex in the presence of the compound.

17. (withdrawn) The method of Claim 16, wherein the stability of the bromodomain-ligand binding complex increases in the presence of the compound and wherein the compound is identified as a stabilizing agent.

18. (withdrawn) The method of Claim 16, wherein the stability of the bromodomain-ligand binding complex decreases in the presence of the compound and the compound is identified as an inhibitor.

19. (withdrawn) The method of Claim 16, wherein the compound is selected by performing rational drug design with the set of atomic coordinates obtained from one or more of Tables 1-6, wherein said selecting is performed in conjunction with computer modeling.

20. (withdrawn) The method of Claim 16, wherein the compound is selected by performing rational drug design with the set of atomic coordinates obtained from a set of atomic coordinates defining the three-dimensional structure of a bromodomain consisting of the amino acid sequence of SEQ ID NO:7, wherein said selecting is performed in conjunction with computer modeling.

21. (withdrawn) A method of identifying a binding partner for a protein that comprises an acetyl-lysine said method comprising:

- (a) contacting the protein with a polypeptide comprising a bromodomain; and
- (b) determining whether the polypeptide binds to the protein; wherein a binding partner for a protein is identified when polypeptide binds to the protein.

22. (withdrawn) The method of Claim 21 wherein the bromodomain has an amino acid sequence from selected from the group consisting of SEQ ID NOs. 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41 and 42.

23. (withdrawn) An agent that can inhibit the binding of a bromodomain with a protein comprising an acetyl-lysine selected from the group consisting of : ISYGR-AcK-KRRQRR (SEQ ID NO:4), ARKSTGG-AcK-APRKQL (SEQ ID NO:5) and QSTSRHK-AcK-LMFKTE (SEQ ID NO:6).

24. (withdrawn) A computer comprising a representation of a Tat-P/CAF complex in computer memory which comprises:

- (a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said data comprises structural coordinates from Tables 10-14;
- (b) a working memory for storing instructions for processing said machine-readable data;
- (c) a central processing unit coupled to said working memory and to said machine-readable data storage medium for processing said machine readable data into a three-dimensional representation of the Tat-P/CAF complex; and
- (d) a display coupled to said central-processing unit for displaying said three-dimensional representation.

25. (withdrawn) A method of identifying a compound that modulates the affinity of P/CAF for Tat that is acetylated at the lysine residue at position 50 of SEQ ID NO:45, said method comprising:

- (a) contacting the bromodomain of P/CAF or a fragment thereof with a binding partner in the presence of the compound, wherein the bromodomain of P/CAF and the binding partner bind in the absence of the compound; and wherein the binding partner is selected from the group consisting of Tat that is acetylated at the lysine residue at position 50 of SEQ ID NO:45, a fragment of Tat comprising an acetyl-lysine at position 50, and an analog of the fragment of Tat comprising an acetyl-lysine at position 50; and
- (b) measuring the affinity of the bromodomain of P/CAF and the binding partner; wherein a compound is identified as a compound that modulates the affinity of the bromodomain of P/CAF for Tat when there is a change in the affinity of the bromodomain of P/CAF for the binding partner in the presence of the compound.

26. (withdrawn) The method of Claim 25, wherein the affinity of the bromodomain of P/CAF for Tat increases in the presence of the compound; wherein the compound is identified as a Tat-P/CAF complex promoting agent.

27. (withdrawn) The method of Claim 25, wherein the affinity of the bromodomain of P/CAF for Tat decreases in the presence of the compound; wherein the compound is identified as an inhibitor of the Tat-P/CAF complex.

28. (withdrawn) The method of Claim 25, wherein the compound is selected by performing rational drug design with the set of atomic coordinates obtained from one or more of Tables 1-5 and 10-14, wherein said selecting is performed in conjunction with computer modeling.

29. (withdrawn) A compound that is a small organic molecule identified by the method of Claim 28; wherein said compound is an analog of acetyl-lysine, but with the proviso that the compound is not included in Figure 13.

30. (withdrawn) A method of identifying a compound that modulates the stability of the binding complex formed between P/CAF and Tat that is acetylated at the lysine residue at position 50 of SEQ ID NO:45, said method comprising:

(a) contacting the bromodomain of P/CAF or a fragment thereof with a binding partner in the presence of the compound, wherein the bromodomain of P/CAF and the binding partner bind in the absence of the compound; and wherein the binding partner is selected from the group consisting of Tat that is acetylated at the lysine residue at position 50 of SEQ ID NO:45, a fragment of Tat comprising an acetyl-lysine at position 50, and an analog of the fragment of Tat comprising an acetyl-lysine at position 50; and

(b) measuring the stability of the binding complex between the bromodomain of P/CAF or a fragment thereof and the binding partner; wherein a compound is identified as a compound that modulates the stability of the Tat-P/CAF complex when there is a change in the stability of the binding complex between the bromodomain of P/CAF or a fragment thereof and the binding partner in the presence of the compound.

31. (withdrawn) The method of Claim 30, wherein the stability of the binding complex between the bromodomain of P/CAF or a fragment thereof and Tat or a fragment of Tat increases in the presence of the compound; wherein the compound is identified as a stabilizing agent.
32. (withdrawn) The method of Claim 30, wherein the stability of the binding complex between the bromodomain of P/CAF or a fragment thereof and Tat or a fragment of Tat decreases in the presence of the compound; wherein the compound is identified as an inhibitor.
33. (withdrawn) The method of Claim 30, wherein the compound is selected by performing rational drug design with the set of atomic coordinates obtained from one or more of Tables 1-5 and 10-14, wherein said selecting is performed in conjunction with computer modeling.
34. (withdrawn) A compound that is a small organic molecule identified by the method of Claim 33; wherein said compound is an analog of acetyl-lysine, but with the proviso that the compound is not included in Figure 13.
35. (withdrawn) An agent that can modulate the binding of P/CAF and Tat; wherein said agent is an analog of acetyl-lysine, but with the proviso that the agent is not included in Figure 13.
36. (withdrawn) The agent of Claim 35 that inhibits and/or destabilizes the binding of P/CAF and Tat.